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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,711	01/17/2002	Yunxiang Zhu	ZHUY 8216US	8638

22852 7590 01/12/2005

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,711	ZHU, YUNXIANG	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment and remarks received on 10/18/2004 has been entered in view of the RCE request. Claims 1-22 have been cancelled. New claims 23-40 have been added. Claims 23-40 are currently pending in this application.

Minor objections

(1) In claim 23, the phrase "a oligosaccharide" should be replaced by the phrase "an oligosaccharide".

(2) Claim 34 is objected to because of the following informalities:

In claim 34 the bond between sugar chain and "M" is missing.

(3) The phrase "M6P" should be written out in full form at least once in the claims.

Appropriate correction is required.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-40 are rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention of record.

In claim 23 in the absence of the chemical formula or name of "a oligosaccharide" and "a compound containing a carbonyl-reactive group" used in a method for coupling a oligosaccharide to a lysosomal enzyme, render the claims indefinite wherein applicant fails to articulate by chemical name or structural formula, requisite to identify "a oligosaccharide" and "a compound containing a carbonyl-reactive group" used in a method for coupling a oligosaccharide to a lysosomal enzyme. Applicant characterizes

the oligosaccharide by requiring a phosphorylated hexose, however the size and additional components are not particularly pointed out in the claims. Likewise, the description of a derivitizing agent as "a compound containing a carbonyl-reactive group" are not particularly pointed out in the claims.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 23-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolvanen et al. (J.B.C., 261,20, 9546-9551, 1986) in view of Monsigny et al. (U.S. Patent 6,251,858).

The claims 23-40 are directed to a method for coupling an oligosaccharide comprising a phosphorylated hexose to a lysosomal enzyme, comprising the steps of: derivatizing an oligosaccharide comprising a phosphorylated hexose with a chemical compound containing a carbonyl-reactive group; oxidizing the lysosomal enzyme to

generate at least one carbonyl group on the lysosomal enzyme; and reacting the the derivatized oligosaccharide with the oxidized lysisomal enzyme thereby coupling the oligosaccharide to the lysosomal enzyme.

Additional claim limitations set forth in dependent claims include the oxidizing agent periodate or galactose oxidase; lysosomal enzyme is chosen from beta-glucocerebrosidase, alpha-galactosidase A, acid- alpha-glucosidase, alpha-N-acetylglucosaminidase and beta-glucuronidase; phosphorylated mannopyranosyl oligosaccharide contains at least one mannose 6-phosphate of the general formula 6-P-M_n-R and includes biantennary or triantennary mannopyranosyl oligosaccharide containing bis-M6P or tri-M6P, phosphorylated mannopyranosyl oligosaccharide can be replaced with oligosaccharides containing the terminal hexoses such as galactose, mannose ,GlcNAc and fucose ; the chemical compound containing carbonyl-reactive groups comprises a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound; and a cyanoborohydride reagent to reduce the hydrazone bond.

Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates (see abstract). Tolvanen et al. disclose that a hydrazine derivative of any available carbohydrate can be introduced into oxidized cell surface glycoconjugates (see page 9546, 2nd col., 4th para.). The glycosylhydrazines of the blood group A active heptasaccharide (containing gal, GlcNAc and fucose) were coupled to periodate-oxidized cells in supplemental material col.1-2 (see coupling of glycosylhydrazines to erythrocytes and K562 cells). Tolvanen et al. also

disclose the use of mannosylhydrazine in the coupling reaction (see page 9547, fig. 11 and 2nd. para). While Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates, Tolvannen et al. differs from applicant's process in that Tolvannen et al. do not suggest the coupling of a oligosaccharide to a glycoprotein such as lysosomal enzyme.

Monsigny et al. teach the coupling of derivatives of oligosaccharides by covalent means to a protein (see abstract). Monsigny et al. disclose proteins in particular the glycosyltransferases, exoglycosidases or endoglycosidases (col.1, line 34). Monsigny et al. disclose the biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate (see col. 16, g, lines 43-54). Monsigny et al. disclose the oligosaccharides containing the terminal hexoses such as galactose, mannose, GlcNAc and fucose (see col. 15, lines 30-50). Monsigny et al. also disclose the use of sodium cyanoborohydride to reduce the imine formed between the reducing sugar and the amine (col.3, lines 28-33).

Therefore, one of ordinary skill in the art would have found the applicants claimed method of coupling a oligosaccharide to a glycoprotein such as lysosomal enzyme, to have been obvious at the time the invention was made having the above cited references before him. Since Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates and Monsigny et al. discloses the coupling of biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate to a protein such in particular the

glycosyltransferases, exoglycosidases or endoglycosidases, one skilled in the art would have a reasonable expectation for success in combining the process steps of the references to accomplish a method for coupling an oligosaccharide derivative by reacting with the oxidized protein to form covalent bond between the oligosaccharide and glycoprotein such as lysosomal enzyme. The motivation for doing so is provided by Tolvanen et al., which suggests that the glycosylhydrazines derivative can be covalently coupled into the oxidized cell surface glycoproteins without affecting their biological actvities (see page 9546, col. 2, 3rd. para.).

Response to Arguments

Applicant's remarks filed on 10/18/04 traversing the prior art rejection under 35 U.S.C 103(a) of the Office Action dated 04/16/2004 have been fully considered but they are not persuasive.

Applicant argues that "neither Tolvanen nor Monsigny teaches or suggests coupling oligosaccharides to oxidized lysosomal enzymes, as required by claims 23-40". It is noted that claim 1 is directed to a method comprising derivatizing a highly phosphorylated mannopyranosyl oligosaccharide compound with a chemical compound containing at least one carbonyl-reactive group; oxidizing a glycoprotein to generate at least one carbonyl group on the glycoprotein; and reacting the said glycoprotein with the said oligosaccharide compound. Tolvanen teaches that a carbohydrate structure can be introduced into cell surface glycoproteins and glycolipids by treating a carbohydrate with hydrazine (a chemical compound containing carbonyl group) to generate a derivative

such as mannosylhydrazine which is reacted with an oxidized glycoprotein wherein the glycoconjugates moiety of a glycoprotein can be oxidized with periodate to generate a carbonyl group on the glycoprotein (page 9546, 2nd col., 3rd para. and page 9547, Fig. 11) and Monsigny et al. teach the coupling of derivatives of oligosaccharides by covalent means to a protein in particular the glycosyltransferases, exoglycosidases or endoglycosidases (col.1, line 34). Indeed, the examiner has established a prima facie case of obviousness rendering claims 23-40 rejected under 35 U.S.C. 103(a) by addressing sufficiently all of the limitations set forth in the instant claims, one skilled in the art would have a reasonable expectation for success in combining the above said references to accomplish a method for coupling a oligosaccharide to a glycoprotein such as lysosomal enzyme.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
January 4,2004